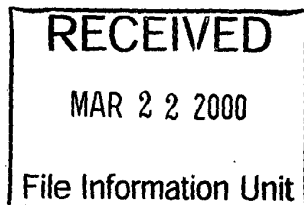


## REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)



In re Application of

BENDIG

Application Number

08/186269

Filed

1-25-94

Class or Unit

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Paper No. 16

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- ☒ (A) referred to in United States Patent Number 5840299, column \_\_\_\_\_
- ☐ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, on page \_\_\_\_\_ of paper number \_\_\_\_\_
- ☐ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, or
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US005840299A

**United States Patent** [19]**Bendig et al.**[11] **Patent Number:** **5,840,299**[45] **Date of Patent:** **Nov. 24, 1998**[54] **HUMANIZED ANTIBODIES AGAINST  
LEUKOCYTE ADHESION MOLECULE  
VLA-4**[75] **Inventors:** Mary M. Bendig, London; Olivier J. Léger, Hertfordshire; José Saldanha, Enfield Middlesex; S. Tarran Jones, Radlett, all of United Kingdom; Ted A. Yednock, Fairfax, Calif.[73] **Assignee:** Athena Neurosciences, Inc., South San Francisco, Calif.[21] **Appl. No.:** 561,521[22] **Filed:** Nov. 21, 1995**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 186,269, which is a continuation-in-part of PCT/US95/01219 Jan. 25, 1995, abandoned.

[51] **Int. Cl.<sup>6</sup>** ..... **A61K 39/395**; C07K 16/28; C12P 21/08; C12N 15/13[52] **U.S. Cl.** ..... **424/133.1**; 424/130.1; 424/141.1; 424/143.1; 424/144.1; 424/153.1; 424/154.1; 424/173.1; 435/7.1; 435/7.2; 435/7.21; 435/7.24; 435/69.6; 435/172.3; 435/251.3; 435/320.1; 530/387.3; 530/388.73; 530/388.75; 530/388.22; 536/23.53[58] **Field of Search** ..... 424/130.1, 133.1, 424/141.1, 143.1, 144.1, 153.1, 154.1, 173.1; 435/69.6, 172.3, 252.3, 320.1, 7.1, 7.2, 7.21, 7.24; 536/23.4, 23.5, 23.53; 530/387.1, 387.3, 388.2, 388.22, 388.7, 388.73, 388.75[56] **References Cited****U.S. PATENT DOCUMENTS**5,260,210 11/1993 Rubin et al. .... 435/240.23  
5,530,101 6/1996 Queen et al. .... 530/387.3**FOREIGN PATENT DOCUMENTS**239400 9/1987 European Pat. Off. .... C12N 15/00  
330506 8/1989 European Pat. Off. .... C07K 15/06  
WO 90/07861 7/1990 WIPO ..... C12P 21/00  
WO 91/03252 3/1991 WIPO ..... A61K 37/10  
91/05038 4/1991 WIPO ..... C12N 5/06  
WO 93/15764 8/1993 WIPO ..... A61K 39/395**OTHER PUBLICATIONS**Lisak et al. J. Neurol. Sciences 62: 281-293 (1983).  
Teitelbaum et al. PNAS 89: 137-141 (1992).  
Weiner et al. Science 259: 1321-1324 (1993).  
Racke et al. J. Neuroimmunol. 46: 175-184 (1993).  
Karussis et al. PNAS 90: 6400-6404 (1993).Cannella et al. Ann Neurol. 37: 424-435 (1995).  
Washington et al. Ann Neurol 35: 89-97 (1994).  
Dore-Duffy et al. in Frontiers in Cerebral Vascular Biology: Transport and its Regulation (eds) Dreues and Betz Plenum Press Ny 1993 pp. 243-248.Monshizadegan et al., "VLA-4-dependent adhesion activities of U937 cells and guinea pig bronchoalveolar lavage leukocytes", 1993, *Agents Actions* 39, pp. C177-C179.Kettleborough et al., "Humanization of a mouse monoclonal antibody by CDR-grafting the importance of framework residues on loop conformation", 1991, *Protein Engineering*, vol. 4, No. 7, pp. 773-783.Yednock et al. "Prevention of experimental autoimmune encephalomyelitis by antibodies against  $\alpha 4 \beta 1$  integrin", 1991, *Letters to Nature*, vol. 356, pp. 63-66.W. J. Harris and S. Emery, "Therapeutic antibodies—the coming of age", 1993, *Tibtech*, vol. 11, pp. 42-45.S. C. Emery and J. R. Adair, "Humanised monoclonal antibodies for therapeutic applications", 1994, *Exp. Opin. Invest. Drugs*, vol. 3, pp. 241-251.S. M. Edgington, "How Sweet It Is: Selectin-Mediating Drugs", 1992, *Bio/Technology*, vol. 10, pp. 383-389.Elises et al., "VCAM-1 on Activated Endothelium Interacts with the Leukocyte Integrin VLA-4 at a Site Distinct from the VLA-4/Fibronectin Binding Site", 1990, *Cell*, vol. 60, pp. 577-584.Dijkstra et al., "Multiple sclerosis: some possible therapeutic opportunities", 1993, *Tips Reviews*, vol. 14, pp. 124-129.A. Mountain and J.R. Adair, "Engineering Antibodies for Therapy", 1992, *Biotech Genetic Engineering Reviews*, vol. 10, pp. 10-13.P.A. Ward and M.S. Mulligan, "Blocking of adhesion molecules in vivo as anti-inflammatory therapy", 1994, *Therapeutic Immunol.*, vol. 10, pp. 165-171.L. K. Jolliffe, "Humanized Antibodies: Enhancing Therapeutic Utility Through Antibody Engineering", 1993, *Intern Rev Immunol.*, vol. 10, pp. 241-250.

Albelda Faseb J. 8: 504-512 (1994).

Kahan Curr Opin Immunology 4: 553-560 (1992).

Natanson et al. Ann Intern Med. 120: 771-783 (1994).

Dalakas Ann. Neurol. 37(51): 52-513 (1995).

Paul (ed) Fundamental Immunology Raven Press NY 1993 p. 242 only.

**Primary Examiner**—Lila Feisee**Assistant Examiner**—Phillip Gambel**Attorney, Agent, or Firm**—Townsend & Townsend & Crew LLP[57] **ABSTRACT**

The invention provides humanized immunoglobulins that specifically bind to the VLA-4 ligand, and methods of treatment using the same. The methods are particularly useful for treatment of multiple sclerosis.

**29 Claims, 16 Drawing Sheets**